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     FILE 'USPATFULL' ENTERED AT 12:09:24 ON 02 JUN 2003

                  E KITTO G B/IN
L1                3 S E4 OR E5
                  E BURNETT M S/IN
L2             1050 S SALMONELLA/CLM
L3               10 S L2 AND (HETEROLOGOUS ANTIGEN/CLM OR RECOMBINANT ANTIGEN/CLM O
L4               80 S L2 AND (HIV/CLM OR HUMAN IMMUNODEFICIENCY VIRUS/CLM)
L5               56 S L4 AND (VECTOR OR VACCINE)
L6               42 S L5 AND VACCINE
L7               28 S L2 AND (SL3261 OR SL-3261)

     FILE 'MEDLINE' ENTERED AT 12:16:33 ON 02 JUN 2003

                  E KITTO G B/AU
L8               42 S E3
L9                0 S L8 AND SALMONELLA
                  E BURNETT M S/AU
L10               6 S E3 OR E6
L11              81 S SL3261
L12               9 S L11 AND PY=1997
L13               6 S L11 AND PY=1996
L14               4 S L11 AND PY=1995
L15               6 S L11 AND PY=1998
L16               7 S L11 AND (CTL OR CYTOTOXIC)
                  E HONE D M/AU
L17              29 S E3-E5
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L10 ANSWER 5 OF 6 MEDLINE
2001112980 Document Number: 20567968. PubMed ID: 11115694. Potential live vaccines for HIV. Burnett M S; Wang N; Hofmann M; Barrie Kitto G. (Department of Chemistry and Biochemistry, Institute of Molecular and Cellular Biology, The University of Texas at Austin, Austin, TX 78712, USA.) VACCINE, (2000 Nov 22) 19 (7-8) 735-42. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Potential live vaccines for HIV were developed using an Lpp-OmpA system to target an HIV antigen, reverse transcriptase, or an immunodominant epitope of this enzyme, to the outer membrane of an attenuated strain of Salmonella SL3261. These live vaccines were administered orally to mice, and fecal IgA and helper T cell responses were measured. Results indicated a fecal IgA response specific to HIV reverse transcriptase, as well as a reverse transcriptase-specific helper T cell response, as measured by proliferation assays. Additionally, tests with the epitope vaccines showed a selective cytotoxic CD8 T cell response. These results suggest that this method of antigen targeting to the outer membrane of attenuated bacterial vectors is very promising not only for HIV vaccine development, but also for antigens from other viral or bacterial pathogens, which could be inserted into the Lpp-OmpA protein construct, to elicit mucosal IgA and T cell responses.

L14 ANSWER 1 OF 4 MEDLINE
96363710 Document Number: 96363710. PubMed ID: 8719522. Construction and immunogenicity of Salmonella typhimurium vaccine vectors that express HIV-1 gp120. Fouts T R; Tuskan R G; Chada S; Hone D M; Lewis G K. (Department of Geographic Medicine, School of Medicine, University of Maryland at Baltimore 21201, USA.) VACCINE, (1995 Dec) 13 (17) 1697-705. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Since the human immunodeficiency virus (HIV-1) is transmitted either parenterally or sexually, both mucosal and systemic immune responses may be required to provide protective immunity. Attenuated Salmonella vectors expressing heterologous antigen can stimulate responses in both compartments. To evaluate the utility of Salmonella vectors as an HIV-1 vector vaccine, a gene expression cassette encoding recombinant HIV-1 gp120 (rgp120) was integrated into the hisOGD locus of Salmonella typhimurium aroA strain, SL3261 (SL3261::120). To test if increased antigen expression potentiates immunogenicity, strains were constructed that express rgp120 from a multicopy asd-stabilized plasmid (SL7207 pYA:120). Immunoblot analysis demonstrated that SL7207 pYA:120 expressed approximately 50-fold more rgp120 than SL3261 ::120. Oral immunization of BALB/c mice with these strains did not stimulate an env-specific CTL response or a significant rise in antigp120 antibody titer as compared to controls. However, splenic T cells from SL7207 pYA::120 immunized mice proliferated upon restimulation with gp120 in vitro while splenocytes from SL3261::120 immunized mice did not, gp120 restimulated splenic T cells from SL7207 pYA:120 immune mice also produced IFN-gamma but no IL-5. Two conclusions can be drawn from these results. First, high level expression of rgp120 in Salmonella vectors is necessary to stimulate a gp120-specific immune response in mice. Second, Salmonella::rgp120 stimulates a gp120-specific Th1 response in mice. This is the first report to describe the construction of a Salmonella::rgp120 vector vaccine that is immunogenic in mice.

L17 ANSWER 19 OF 29 MEDLINE
96065464 Document Number: 96065464. PubMed ID: 7483777. Construction and characterization of a Salmonella typhi-based human immunodeficiency virus type 1 vector vaccine. Fouts T R; Lewis G K; Hone D M. (Department of Geographic Medicine, School of Medicine, University of Maryland at Baltimore 21201, USA.) VACCINE, (1995 Apr) 13 (6) 561-9. Journal code: 8406899. ISSN: 0264-410X. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Since the human immunodeficiency virus type 1 (HIV-1) is transmitted either parenterally or sexually, both systemic and mucosal immune responses might be required to provide protective immunity. One option is to express HIV proteins in attenuated Salmonella vectors that elicit immune responses in both compartments. The first step to constructing such a strain was achieved by integrating a gene expression cassette encoding recombinant HIV-1 gp120 (rgp120) into the aroC locus of an attenuated vaccine strain of S. typhi. This rgp120 expression cassette utilizes the strong constitutive promoter, P1pp/lacUV5, and produces rgp120 to 0.05-01% of the total bacterial cell protein. Immunoblot analysis shows that the S. typhi strains containing the integrated cassette express a protein that is both recognized by anti-gp120 monoclonal antibodies (mAbs) and is the appropriate size for nonglycosylated full-length gp120 (52 kDa). Immunoblot analysis also demonstrates that the recombinant S. typhi strains express the rgp120 as monomers and multimers found predominantly in the insoluble fraction of the bacteria. Antigen-capture ELISA, using antibodies specific for continuous epitopes on gp120, revealed that the exposure of these epitopes on S. typhi-expressed rgp120 differs from exposure of these epitopes on baculovirus-expressed rgp120 that binds CD4. Epitopes in the first conserved region (109-113) and the third conserved/fourth variable regions (376-380, 382-384, 395-400) are more "surface-exposed", while one epitope in the third variable region (313-324) is more "buried" relative to the corresponding epitopes of baculovirus expressed gp120. Antibodies recognizing discontinuous epitopes of the CD4 binding domain do not react with the S. typhi expressed rgp120.(ABSTRACT TRUNCATED AT 250 WORDS)

L17 ANSWER 14 OF 29 MEDLINE
97454210 Document Number: 97454210. PubMed ID: 9310285. Induction of mucosal and systemic responses against human immunodeficiency virus type 1 glycoprotein 120 in mice after oral immunization with a single dose of a Salmonella-HIV vector. Wu S; Pascual D W; Lewis G K; Hone D M. (Division of Infectious Diseases and Gastroenterology, School of Medicine, Johns Hopkins University, Baltimore, Maryland 21202, USA.) AIDS RESEARCH AND HUMAN RETROVIRUSES, (1997 Sep 20) 13 (14) 1187-94. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.

AB Previous studies from our group showed that a Salmonella-HIV vector vaccine that expressed recombinant HIV-1 envelope protein gp120 stably in the vector cytoplasm elicited type 1 helper T cell (Th1) responses to gp120. Despite the promise of such vaccines, a major limitation in their use was that multiple immunizations were required to elicit even small responses. For this reason, we sought a modified vector configuration that would induce more potent gp120-specific T cell responses exhibiting a broader spectrum of effector functions after a single inoculation. In this article we describe the construction and immunogenicity of a Salmonella-HIV vector that displays a truncated derivative of HIV-1(IIIB) envelope in the periplasm of the vector. A single oral dose of this Salmonella vector, called H683(pW58-asd+), generated a gp120-specific proliferation response in the spleen 14 days after immunization. In

agreement with our previous findings, the gp120-specific splenic CD4+ T cells elicited by H683(pW58-asd+) displayed a Th1 phenotype; however, gp120-specific splenic CD4+ Th2 cells were also evident. In addition, this strain induced strong gp120-specific IgA antibody-secreting cell (ASC) responses in the intestinal lamina propria and mesenteric lymph nodes. As many as 2% of the total lamina propria and mesenteric lymph node IgA ASCs were found to be specific for gp120 28 days after a single oral dose of H683(pW57-asd+). Because the proliferative response following a single dose of H683(pW58-asd+) was comparable to that seen previously after three doses of an analogous construct expressing recombinant gp120 in the cytoplasm, these observations suggest that Salmonella-vectored secreted HIV-1 antigens elicit higher T cell responses than their cytoplasmically bound analogs.

L17 ANSWER 5 OF 29 MEDLINE
2001567684 Document Number: 21530470. PubMed ID: 11672930. Mucosal and systemic HIV-1 Env-specific CD8(+) T-cells develop after intragastric vaccination with a Salmonella Env DNA vaccine vector. Shata M T; Reitz M S Jr; DeVico A L; Lewis G K; Hone D M. (Virology Laboratory, Lindsley F. Kimball Research Institute, New York Blood Center, New York, NY 10021, USA.) VACCINE, (2001 Nov 12) 20 (3-4) 623-9. Journal code: 8406899. ISSN: 0264-410X. Pub. country: England: United Kingdom. Language: English.

AB CD8(+) T-cell responses provide beneficial antiviral immunity against human immunodeficiency virus 1 (HIV-1). In this study, we show that intragastric vaccination with a Salmonella HIV-1 Env DNA vaccine vector generates Env-specific CD8(+) T-cells, both in mucosal and systemic lymphoid tissue. By contrast, intramuscular vaccination with the Env DNA vaccine alone only induced systemic CD8(+) T-cells. To our knowledge, this is the first report showing both mucosal and systemic CD8(+) T-cell responses following vaccination with a Salmonella vaccine vector. These data suggest that this mode of HIV-1 DNA vaccine delivery will be advantageous over parenterally administered HIV-1 DNA vaccines.

L17 ANSWER 3 OF 29 MEDLINE
2002389688 Document Number: 22133711. PubMed ID: 12096189. A Tat subunit vaccine confers protective immunity against the immune-modulating activity of the human immunodeficiency virus type-1 Tat protein in mice. Agwale S M; Shata M T; Reitz M S Jr; Kalyanaraman V S; Gallo R C; Popovic M; Hone D M. (Division of Vaccine Research, Institute of Human Virology, University of Maryland Biotechnology Institute, Baltimore, MD 21202, USA.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2002 Jul 23) 99 (15) 10037-41. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.

AB The rational design of new therapies against HIV-1 necessitates an improved understanding of the mechanisms underlying the production of ineffective immune responses to HIV-1 in most infected individuals. This report shows that the CD8(+) T cell responses to gp120 were greatly diminished in mice vaccinated with a bicistronic gp120-Tat DNA vaccine, compared with those induced by a DNA vaccine encoding gp120 alone. The CD8(+) T cell responses induced by the latter included strong gp120-specific IFN-gamma secretion and protective antiviral immunity against challenge by a vaccinia-env pseudotype. The degree to which Tat influenced CD8(+) T cell responses depended on the bioactivity of Tat. Thus, a bicistronic DNA vaccine that expresses gp120 and a truncated Tat defective for LTR activation elicited strong IFN-gamma -secreting CD8(+) T cell responses to gp120 but conferred only marginal protection against the

vaccinia-env challenge. The effect of Tat was completely blocked, however, by immunization with inactivated Tat protein before vaccination with the bicistronic gp120-Tat DNA vaccine.